

Review

Structure and Applications of Pectin in Food, Biomedical, and Pharmaceutical Industry: A Review

Cariny Maria Polesca Freitas ¹, Jane Sélia Reis Coimbra ², Victor Gomes Lauriano Souza ³
and Rita Cássia Superbi Sousa ^{1,*}

¹ Department of Chemistry, Federal University of Viçosa (UFV), Av. Peter Henry Rolfs s/n, Viçosa 36570-900, Brazil; carinypolesca@gmail.com

² Department of Food Technology, Federal University of Viçosa (UFV), Av. Peter Henry Rolfs s/n, Viçosa 36570-900, Brazil; jcoimbra@ufv.br

³ International Iberian Nanotechnology Laboratory (INL), Av. Mestre José Veiga s/n, 4715-330 Braga, Portugal; victor.souza@inl.int

* Correspondence: rita.sousa@ufv.br

Abstract: Pectin is a biocompatible polysaccharide with intrinsic biological activity, which may exhibit different structures depending on its source or extraction method. The extraction of pectin from various industrial by-products presents itself as a green option for the valorization of agro-industrial residues by producing a high commercial value product. Pectin is susceptible to physical, chemical, and/or enzymatic changes. The numerous functional groups present in its structure can stimulate different functionalities, and certain modifications can enable pectin for countless applications in food, agriculture, drugs, and biomedicine. It is currently a trend to use pectin to produce edible coating to protect foodstuff, antimicrobial bio-based films, nanoparticles, healing agents, and cancer treatment. Advances in methodology, use of different sources of extraction, and knowledge about structural modification have significantly expanded the properties, yields, and applications of this polysaccharide. Recently, structurally modified pectin has shown better functional properties and bioactivities than the native one. In addition, pectin can be used in conjunction with a wide variety of biopolymers with differentiated properties and specific functionalities. In this context, this review presents the structural characteristics and properties of pectin and information on the modification of this polysaccharide, its respective applications, perspectives, and future challenges.

Keywords: by-products; extraction; food; pectin applications; polysaccharide; structural modification



Citation: Freitas, C.M.P.; Coimbra, J.S.R.; Souza, V.G.L.; Sousa, R.C.S. Structure and Applications of Pectin in Food, Biomedical, and Pharmaceutical Industry: A Review. *Coatings* **2021**, *11*, 922. <https://doi.org/10.3390/coatings11080922>

Received: 12 July 2021

Accepted: 28 July 2021

Published: 1 August 2021

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1. Introduction

Biopolymers are highly attractive once they are renewable and with relatively low cost to produce. They are commonly studied for food, pharmaceutical, and biomedical applications [1–3]. The global biopolymers market is expected to reach \$27.9 billion by 2025 [4]. Pectin, a water-soluble anionic biopolymer, stands out among the most commercialized biopolymers [5]. The global pectin market, estimated at \$1 billion in 2019, is expected to reach \$1.5 billion in 2025 [6].

Pectin is a structural polysaccharide of the cell wall of plants [5], known to be a macromolecule of high molecular weight, which can be transformed into a hydrogel and form a flexible network of polymer chains [7]. Commercial pectin is commonly extracted from apples and citrus fruits. However, researches have been focused on the extraction of pectin from various industrial by-products, which presents itself as a green option for the valorization of agro-industrial residues, in line with the concept of circular bioeconomy [5,8–10].

Pectin has a complex structural formed by homogalacturonan (HG), rhamnogalacturonan I (RGI), rhamnogalacturonan II (RGII), and xylogalacturonan (XG) [11]. Despite common characteristics, pectins can exhibit diverse structures varying according to the

source and extraction method [12–14]. In this sense, note that pectin is susceptible to physical, chemical, and/or enzymatic changes. The numerous functional groups present in the pectin structure can stimulate different functionalities, and certain modifications enable pectin for numerous applications [13,15,16], mainly because it is a product considered safe, non-toxic, with low production cost and high availability [5].

The literature data on pectin mainly address its applications in food, agriculture, medicines, and biomedicine, with a trend in the production of edible food coatings, bio-based antimicrobial films, and nanoparticles for studies in the treatment of cancer; in the healing of wounds; and dressings by the pharmaceutical industry [5,17–19].

The possibility of modifying its structure makes it possible to use pectin in new functions, either alone or in combination with other biopolymers. This material with high added value and differentiated behavior has aroused the interest of industry and research. Thus, this review brings together the most recent published information on this polysaccharide, focusing on the detailed description of their structure and how they can be modified according to the different extraction processes and their possible applications and future trends.

2. Pectin Structure

The cell wall of primary plants (Figure 1) mainly comprises three classes of polysaccharides: cellulose, hemicellulose, and pectin [16,20], which can also be located on the middle lamella of upper plants [9,15,21]. Pectin represents a family of complex polysaccharides that play important roles in plant growth and development, such as mechanical resistance and barrier against the external environment [14]. The cell wall is considered biphasic: the crystalline cellulose microfibrils tied by the hemicellulose are submerged in a matrix similar to pectin and protein gel. The way in which these components are associated with a coherent material remains unknown [22].

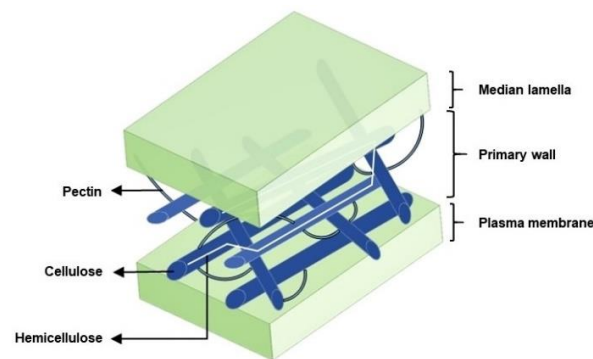


Figure 1. The cell wall of primary plants. Adapted from Raven et al. [23].

Pectin has a complex structure (Figure 2) composed of its sub-domains, rhamnogalacturonan I (RGI), rhamnogalacturonan II (RGII), and xylogalacturonan (XG), attached to the homogalacturonan (HG) skeleton (information in Table 1) [11]. According to the Food and Agriculture Organization (FAO), the structure of pectin must contain $\geq 65\%$ galacturonic acid (GalA) [15]. The relation between the units of GalA esterified with methyl and the total units of GalA in the HG skeleton represents the degree of esterification (DE) [9,16,24].

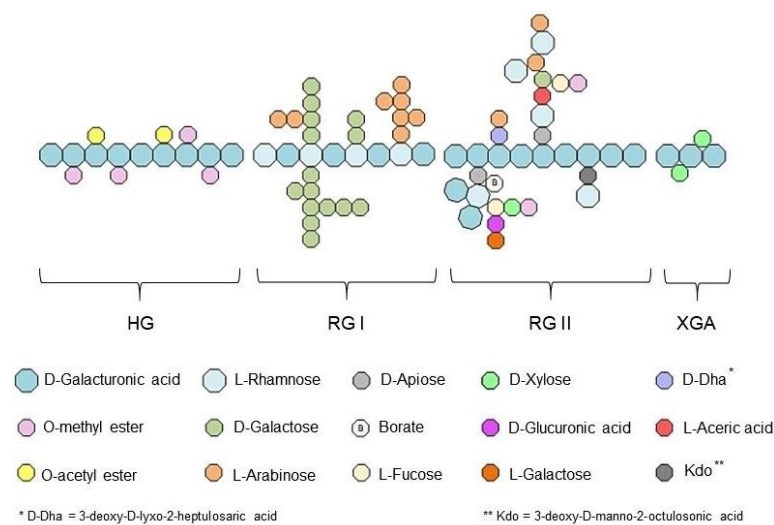


Figure 2. Chemical structure of the pectin molecule. Adapted from Maxwell et al. [25], Marenda et al. [26], Mohnen [27], and Wang et al. [14].

Table 1. Pectin structural composition.

Sub-Domains Title	Amount (%)	Structural Composition	Ref
Homogalacturonan (HG)	65	Linear homopolymer of GalA partially esterified with methyl esters (α 1-4 bonded) at the C-6 position and acetyl esters at the O-2 and/or O-3 positions.	[9,12,13,15,25,27,28]
Rhamnogalacturonan I (RGI)	20–35	-Repeated disaccharides composed of GalA residues and rhamnose (Rha); -Rha residues (20% to 80%) can be replaced by neutral sugar side chains (galactose, arabinose, xylose, and apiosis).	[9,12,13,15,25,27,28]
Rhamnogalacturonan (RG II)	<10	-HG backbone composed of GalA (7–9 units) where complex branches made up of 12 types of monosaccharides (including monomers such as apiose, fucose, acetic acid, DHA, or KDO) can exist.	[13,15,25,27,28]
Xilogalacturonan (XG)	<10	Highly complex branched structure linked through a β -glycoside bond with GalA's O-3 in HG.	[13,25]

GalA = galacturonic acid.

Pectins are classified as high degree of esterification (HM) ($DE > 50\%$) or low degree of esterification (LM) ($DE \leq 50\%$), having distinct properties and different industrial applications [14]. HM pectins form gels in solutions with a high concentration of soluble solids and acid medium ($pH < 3.5$), which are stabilized by intermolecular hydrogen bonds and hydrophobic bonds between methyl esters. They are generally used in the production of jellies, sweets, and desserts. LM pectins form gels over a wide pH range (2.0–6.0) with the proper concentration of calcium ions or multivalent cations [5,14,16,26], for example, Ca^{2+} ions. The concentration of calcium required for gelation depends on the pH and soluble solids [29]. Ionic interactions are dominant between polyvalent cations and free carboxyl groups in galacturonic acid residues for gelation [30]. They are commonly used in water-soluble soy extract, as well as in dietary and dairy products [26]. HM pectins can be transformed into LM through chemical de-esterification by alkali or enzymatic treatment by pectin methylesterase [30].

Despite common characteristics, pectins can exhibit diverse structures, which vary according to the source and method of extraction, namely, molecular mass and its distributions; degree of esterification; neutral sugar side chains; the presence of ferulic acid; proteins; and methoxylation and acetylation degrees, to mention a few [12–14,16]. These characteristics significantly influence the gel-forming property and the functionality of the pectin [5,11]. Among the technical-functional properties that pectins provide to products, it is worth mentioning its ability to easily dissolve in basic medium and form gels in acidic medium, which are interesting properties for drug administration applications. The mucoadhesive or antimetastatic properties are interesting for the formation of mechanically stable gels. In addition, pectin exhibits several antimicrobial and antiviral properties, water solubility decreases, and mechanical properties increase [5]. Numerous researches have provided substantial evidence of excellent emulsifying, gelling, foaming, and film-forming properties [11,31].

Regarding the parameters for pectin extraction from beet pulp under different conditions of pH (1, 1.4, and 1.8), temperature (75, 85, and 95 °C), and time (2, 3, and 4 h), Chen et al. observed that changes in pectin extraction conditions caused significant changes in the contents of protein (0.5% to 6%), galacturonic acid (56.0% to 80.1%), and ferulic acid (1.5% to 2.4%) [32].

Commonly, chemical analyzes of pectin extracts reveal the presence of proteins, which are considered contaminants or inherent parts of the polymer, as the primary cell wall of plants contains polysaccharides and structural proteins. Proteins are preferentially bound to neutral sugar side chains [15,16].

Considering that pectin is a complex polysaccharide, the identification and characterization of its chemical structure are carried out by analytical tools such as Fourier Transform Infrared Spectroscopy (FTIR) [8], FT-Raman Spectroscopy [33], Nuclear Magnetic Resonance (NMR) spectroscopy [34], Gas Chromatography Mass Spectrometer (GC-MS) [14], High-Performance Liquid Chromatography (HPLC), carbohydrate gel electrophoresis (PACE) [35], and electrospray ionization mass spectroscopy (ESIMS) [36].

3. Changes in the Structure of Pectin

Pectin exhibits diversity in its molecular structure and is susceptible to physical, chemical, and/or enzymatic changes. The different functional groups present in the pectin structure can stimulate different functionalities, and certain modifications can enable this polysaccharide for novel applications due to changes in physical-chemical properties such as formal charge, degree of esterification, and molecular weight [13,15,16].

Recent research points out that pectin derivatives with reduced molecular weight present new functional groups, which may result in novel applications to the use of this polysaccharide, i.e., an expansion of pectin applications [37]. The class of modified pectins (MP) (i) has more galactoside residues than xylan and arabinan; (ii) contains fragments rich in RGI domains [13]; (iii) presents larger bioactivities and broader applications than the native [38]; (iv) plays a role as a nutraceutical or pharmacist in cancer therapy, due to its ability to protect the immune system, regulate oncogenes, promote the growth of probiotics and inhibit the development of tumors [14]; and (v) revealed numerous pharmaceutical bioactivities, including wound healing, induction of apoptosis in human cancer cells, antimetathesis, anti-ulcer, anti-obesity, anticoagulant and cholesterol-lowering effects [14,38], and lipase inhibition, in clinical trials with swine pancreatic lipase [39].

The modification of pectin can be carried out using demethylesterification techniques (chemical and enzymatic), substitution (alkylation, amidation, thiolation, and sulfation), chain elongation (crosslinking and grafting), and depolymerization (enzymatic modification and alkaline treatment) [16,25,40,41]. Note that these conventional modification methods may present disadvantages due to the high cost of treatment, high time, a limited degree of hydrolysis, and uncontrolled reduction in molecular weight. Chemical methods, which depend on high temperatures and the use of acids, are related to environmental pollution and, therefore, non-thermal and efficient technologies aroused and are currently

being investigated. As a “green and emerging” technology, ultrasound is being used for structural modification of pectin, which has proven to be an effective tool by providing the reduction of molecular mass, control of the extent of depolymerization, reduction of the processing time, and increase of its bioactivity, in addition to being simple and fast [14,37,42,43].

There are numerous mechanisms associated with pectin modification due to the application of ultrasound, including cavitation, which varies according to the frequency, power intensity, and environment in which the acoustic waves transmit. At the initial moment of ultrasonic power, small bubbles are formed, creating compression and expansion. The energy released during cavitation is based on the kinetics of the growth and collapse of bubbles. The implosion of cavitation bubbles stimulates pyrolysis, causing the cleavage of the bond and the dissociation of water and other gases, leading to the start of a series of radical reactions. The dissociation of water molecules produces $-OH$ and $-H$ radicals and forms hydrogen peroxide (H_2O_2). These radicals can interact with each other and consequently contribute even more to the chemical modification of pectin [14,42,43].

Researchers used ultrasound to degrade and modify pectin from different extraction sources, such as apples [37], sweet potato [38], and citrus fruits [37,44], testing a range of conditions: ultra-sonic frequency (20–45 kHz), time (5–60 min), and temperature (5–50 °C). Combining ultrasound with other extraction methods is also the aim of recent studies, e.g., ultrasonic combined with acid and enzymatic treatment [37], pectinase [45], and Fenton system [44]. According to the results of Muñoz-Almagro et al., the presence of citric and nitric acids increased the depolymerization of pectin, with no significant difference between the two acids. There was an influence of the depolymerization rate for pectin concentration greater than 5% regarding the enzymatic treatment [37]. The research results of Ma et al. indicated that citrus pectin treated by ultrasound and pectinase was hydrolyzed with significantly less time. The authors found that the complex polymeric structures of pectin were transformed into smaller units with simpler branches and shorter chains. The combination of ultrasound and pectinase significantly decreased the DE of the pectin and severely destroyed the HG regions, but protected the RGI domains [45]. The results of the research of Zhi et al. highlighted that the Fenton reaction is a potential advanced oxidation process that uses ferrous ions as a catalyst to continuously generate OH from hydrogen peroxide. Compared to the isolated use of ultrasound and the Fenton system, the joint process had a synergistic impact on the degradation of pectin into smaller fragments, with a closer distribution of molecular weight in a short time. The pectic polysaccharide showed enriched RGI domains and low DE, exhibiting greater antioxidant activity [44].

Currently, researchers like Muñoz-Almagro et al. [37], Chen et al. [43], Wand et al. [46], Qiu et al. [47], Hu et al. [48], Fan et al. [49], and Zheng et al. [50] have been using ultrasound technology to modify pectin, as it is a green non-thermal technology. However, ultrasound technology also has some limitations and drawbacks. One of the most important challenges is the erosion of the ultrasonic probe during long-term processing, which will influence the quality of the final products and the probe's lifetime. An *in vivo* study is necessary to verify the bioavailability of the pectin obtained by ultrasound technology since most studies have focused only on *in vitro* studies. In addition, the expansion of the scale and the possibility of degradation of the ultrasonic probe must receive attention from many perspectives of effectiveness, sustainability, and profitability [14].

4. Pectin Extraction

On an industrial scale, pectin is extracted mainly from the citrus peel (85%), apple pomace (14%), and beetroot (1%) [11,14]. However, current studies report that pectin can be extracted from many by-products of the food industry, making it possible to value agro-industrial waste. Some of the by-products explored in recent years are passion fruit peel [8], mango peels [51], grape marc [52], jackfruit peels [53], kiwi peels [54], potato pulp [9], melon peels [55], watermelon peels [56], coffee pulp [57], cocoa shells [58], banana

peels [59], pomegranate peels [60], durian peels [61], okra pods [62], pumpkin peels [63], and papaya peels [64].

Acid extraction and alcoholic precipitation are commonly used to obtain pectin on an industrial scale, which can be explained by its lack of operational complexity, despite the high energy and solvent costs [9,16,20]. Acid extraction is usually based on the hydrolysis of protopectin at high temperatures [55]. Many researchers have investigated the effects of different acid solvents and extraction conditions (pH, temperature, time, and solid:liquid ratio) in the extraction yield, structure, and physicochemical properties of pectin. Most of the time, sulfuric, hydrochloric, or citric acids were used at high temperatures (60–90 °C) for extended periods (1–6 h), followed by alcoholic precipitation [12,16,65].

In recent years, alternative methods to conventional acid extraction have been studied to overcome the environmental concerns with the generation of effluents residues related to those traditional methods. With the popularization of green chemistry, examples of technologies as novel extraction methods employed include Microwave Assisted Extraction (MAE) [53,66,67], Ultrasound-Assisted Extraction (UAE) [14,68,69], Subcritical Water Extraction (SWE) [70–72], Extraction with Deep Eutectic Solvents (DES) [73,74], Extraction with Natural Deep Eutectic Solvents (NADES) [75], Pulsed Electric Field (PEF) [76], and the combination of these methods [24,77–79]. For more detailed information on alternative methods to conventional pectin extraction, read the reviews of Freitas et al. [16] and Adetunji et al. [80].

5. Applications

Pectin can be used for numerous applications, mainly because it is a safe, non-toxic product with low production cost and high availability [5]; moreover, its functionalities are influenced by its structure [81]. In this sense, detailed topics on the application of pectin are described below.

5.1. Pectin in the Food Industry

Pectin is generally used in the food industry as a gelling, thickening, stabilizing, and emulsifying agent [11,40,65,82]. Pectin forms hydrogels and is therefore widely used in hydrated and viscous foods [83]. Popular for use in jams, fruit juices, desserts, dairy products [84], and jellies, which is why the gelling properties of pectin are well known [85]. The use as a stabilizing agent in colloidal dispersions varies between emulsions, foods fortified with antioxidants, acidified milk drinks, and fruit drinks with high protein content [13,81]. Information on the emulsifying activity of pectin is detailed in Table 2.

Table 2. Information on the emulsifying activity of pectin.

Activity of Pectin	Features and Conditions	Results	Applications	Ref
Emulsifying	The use of pectin as an emulsifying agent is favored by its molecular characteristics (protein portion, acetyl group, acetylation position, ferulic acid content, degree of esterification, neutral sugar side chain, and average molecular weight) and environmental conditions (pectin concentration and pH of the solution). Proteins play the main role to confer emulsifying capacity: the droplet size of pectin-stabilized emulsions decreased (4.12 to 1.5 μm) as the protein content of pectin from beetroot pulp increased (0.5 wt.% to 3 wt.%) [32]. Pectin with the highest protein content exhibited good emulsifying capacity.	<ul style="list-style-type: none"> - Anchor formation by the protein portion: allows the adsorption of pectin on the oil drop surface, decreasing the interfacial tension at the oil/water interface, enhancement and improvements on the emulsion stability due to the protein–oil/water interface binds, allowing the pectin to form a thicker stabilizing layer protecting droplets against aggregation; - Increase the viscosity of the continuous aqueous phase of emulsions, stimulating the restriction of the mobility of the droplets dispersed in the oil, inhibiting or minimizing its tendency to migrate and coalesce; - Use of a low amount of pectin (about 1.5%) as an emulsifier compared to other polysaccharides (4% of soy-soluble polysaccharides and up to 10% of gum arabic). 	<ul style="list-style-type: none"> - Emulsified oils and emulsion-based foods to use in low-fat mayonnaise, fatty dairy products, ice cream, and emulsified meat products; - Emulsified pectin oils as a fat substitute to develop products with low fat and/or low salt content, improving the nutritional quality of food. 	[9,12,13,15,16,32,81,86]

Note that pectin has an antioxidant capacity, which can be attributed to its ability to chelate metal ions. This capacity is affected by the source and method of extraction once it is associated with the pectin DE. The addition of pectin to food emulsions as an antioxidant can favor numerous functionalities and reduce the synthetic additives and achieve clean label products [40,65]. Celus et al. investigated the role of DE modification of citrus pectin and evaluated the physico-chemical and oxidative stability of flaxseed/sunflower emulsions. According to their results, DE significantly influenced the oxidative stability of the emulsions and, the LM pectin ($DE \leq 33\%$) exhibited greater lipid antioxidant activity than the pectin with HM ($DE \geq 58\%$); which shows that pectin can be used as a natural alternative to synthetic antioxidants [40].

Another major application of pectin in the food industry is to produce packaging materials and edible coatings. Its ability to form gels and films explains its use in the development of biodegradable food packaging or edible coatings for food preservation [82,87].

The use of food packaging and edible coatings based on materials derived from petroleum sources are related to the depletion of natural resources [88]. In contrast, pectin coatings have been studied to extend the shelf-life of food products in the last years, principally due to the fact they are renewable, biodegradable, and biocompatible [89]. These features are linked to the 12 green chemistry principle and are very important to reach the sustainable world. In the food products, the coating has a significant effect to control the water loss and reduce decay in fruits, maintaining their firmness and extending their shelf life [90].

Food packaging is responsible for millions of tons of waste in landfills every year, causing a severe impact on the environment [91]. In this sense, the growing concerns about safety and the demand for natural and ecological technologies have been motivating research into sustainable materials for use in food packaging [81,82]. Edible pectin coatings change the atmosphere around the fruits, modifying the oxygen levels inside the fruits and, therefore, limiting physiological degradation. In addition, it also decreases the quality degradation induced by fruit ripening in terms of texture or loss of bioactive compounds during storage [89]. Some studies carried out in recent years with interest in using pectin as an edible coating and food packaging are shown in Table 3.

Table 3. Studies using pectin as an edible coatings and food packaging.

Use of Pectin	Goal	Results	Ref
Films	Films of apple pectin (2%), low-acyl gellan (0.5%) and glycerol (2.2%) incorporated with nisin were produced and the kinetics release was studied (at 5 and 30 °C) from brain heart infusion (BHI) broth and nutrient agar (food simulant) used for cultivation of <i>L. monocytogenes</i> food model to determine the period of film bioactivity and its potential use as an antimicrobial film	<ul style="list-style-type: none"> - At equilibrium time (72 h), 83% of initial nisin was released at 30 °C while it was 81% at 5 °C; - Release patterns of nisin from the pectin-gellan films indicate that these materials can be used as anti-listerial films for prolonging shelf-life of packed food systems; - The incorporation of nisin formulation into the films led to more plasticized films. 	[92]
Films	Citrus high-methoxyl pectin (PEC) films activated by nanoemulsions (NE) of copaiba oil (CP) at 1%, 3%, and 6% (wt. of water) and Tween 80 (1 wt.% of CP) to ultrapure water were evaluated of chemical, morphological, thermal, mechanical and microbial properties	<ul style="list-style-type: none"> - The addition of CP-NE into the films improved their physico-chemical and antimicrobial properties, and increased the film's biodegradation profile; - The active pectin film showed great potential to be used as food packaging. 	[93]
Coating	Edible coating of HM sunflower pectin (1% w/v), with sweeteners: sucrose (10%), stevia or saccharin (concentration 400× lower than sucrose) and their possible combination with two modified atmosphere packs (MAP) to extend the shelf life of strawberries	<ul style="list-style-type: none"> - The coatings, formed only with calcium and stevia or saccharin, prolonged the shelf life of strawberries up to 12 days compared to uncoated fruits by reducing microbial growth, maintaining the fruit firmness, and constant mass loss; - When combined with MAP (10% CO₂, 85% N₂, and 5% O₂), the same edible coatings have extended the shelf life of strawberries up to 23 days. 	[94]

Table 3. Cont.

Use of Pectin	Goal	Results	Ref
Coating	Edible coating of HM pectin from citrus peel (3%) loaded with oregano essential oil (OEO) and resveratrol (RES) nanoemulsion (2% OEO, 5% Tween 80%, 1.6% ethanol and 800 mg/L RES) applied in fresh pork tenderloin and packaged under high oxygen MAP (HOMAP)	<ul style="list-style-type: none"> - The coatings extended the shelf life of the meat, minimizing the change in color and pH, delaying lipid and protein oxidations, maintaining its tenderness, and inhibiting microbial growth during the 20 days of HOMAP packaging at 4 °C; - Incorporation of OEO or resveratrol further increased the preservative effects due to their antioxidant and antimicrobial properties. 	[95]
Films	Films were prepared with LM pectin (2% w/v), glycerol (1.5 g/g of pectin), calcium chloride (0.005 g/g of pectin) and incorporated with acerola alcoholic extract, cashew apple alcoholic extract, strawberry alcoholic extract or the combination of the 3 extracts (0.17 g of total solids/g of pectin).	<ul style="list-style-type: none"> - The films with acerola alcoholic extract exhibits the highest antioxidant capacity retention (DPPH = 98.3, FRAP = 969, and ABTS = 114.24 mg of Trolox/g of dry extract); - The films with acerola alcoholic extract exhibits the highest phenolic compounds (236 mg of GAE/g of dry extract) and vitamin C (8.8 mg of AA/of dry extract). 	[96]
Coating	Edible coatings of fish gelatin (3% w/v), orange peel HM pectin (3% w/v) and glycerol (15%) applied in packaged ricotta cheese stored under refrigeration for 7 days	<ul style="list-style-type: none"> - The coating provided an improvement in the physical-chemical and textural properties of the cheese during storage; - The coating increases the microbial stability of the cheese during refrigerated storage and offers health-promoting benefits to consumers. 	[97]
Films	Packaging material from <i>Citrus junos</i> pomace (CJP) pectin (3% w/v) and a selected plasticizer (fructose, sorbitol, and glycerol) (0.3 g/g CJP) dissolved in water were elaborated in addition of rambutan peel extract (RPE) (0.25%, 0.5%, and 1.0% w/v)	<ul style="list-style-type: none"> - Glycerol was selected as the optimal plasticizer for CJP films; - The CJP without RPE had lower Total Phenolic Content (TPC) (5.08 mg GAE/g film) than the CJP film with 1% of RPE (53 mg GAE/g film); - The CJP prepared in this study can be used as a low-cost active biodegradable film material. 	[98]
Coating	Combinations of HM pectin and corn flour (relation 1:0, 1:1, 4:1, 3:2 v/v) pectin, corn flour and beet powder (with addition of beet powder at concentration 0.4%) to protect tomatoes	<ul style="list-style-type: none"> - All treatments led to a reduction in weight loss compared to untreated tomatoes; - The coating of pectin and corn flour (1:1 v/v) was the best treatment, resulting in less weight loss and a percentage of deterioration. The coated fruits retained their maximum brightness and showed minimal shrinkage of the pericarp at the end of 30 days of storage; - The incorporation of beet powder resulted in greater permeability to water vapor. However, due to the higher solids, coatings with the addition of beet powder were less effective in reducing evapotranspiration. 	[89]
Films	Films from blending of citrus peel low-methylated (7%) PEC and <i>Vicia ervilia</i> proteins concentrate (BVPC) were elaborated by dispersion of 5g of BVPC in 100 mL of distilled water, addition of 50% (w/v protein) glycerol	<ul style="list-style-type: none"> - BVPC/PEC exhibited a tensile strength double (2.90 MPa) than the one observed with films containing only BVPC (1.52 MPa); - The elongation at break resulted higher in the films containing PEC (41.17%) than films containing only BVPC (30.15%), leading to conclude that films are more extensible when PEC occur in the films forming solutions. 	[99]
Coating	Pectin-alginate (PA) coatings (pectin 15 g·L ⁻¹ , sodium alginate 10 g·L ⁻¹ , glycerol 6.75 g·L ⁻¹ , sodium bicarbonate 2 g·L ⁻¹) and a mixture of PA and ethyl lauroyl arginate (PAL) to eliminate cross-contamination of enteritidis by <i>Salmonella</i> spp. on fresh eggs	<ul style="list-style-type: none"> - Eggshells treated with PA and PAL coatings had a significantly smaller microbial population compared to uncoated eggshells; - PA and PAL coatings effectively inhibited the growth of <i>Salmonella</i> spp. after 1 and 7 days of storage, respectively. 	[100]

Table 3. Cont.

Use of Pectin	Goal	Results	Ref
Coating	Solutions of industrial citrus pectin (1%, 3%, 5%, and 8%) used as an edible coating for fresh strawberries	<ul style="list-style-type: none"> - Pectin coatings samples showed better behavior in terms of color variation than control; which indicates the positive effect of the coatings as a selective barrier, preventing the exposure of the fruit to environmental oxygen and inhibiting possible oxidation reactions; - All samples had a considerable loss of moisture during storage. 	[101]
Films	Films were produced using pectin (0.8%–1.8% w/v) extracted from byproduct of <i>Hibiscus sabdariffa</i> L. (HsL) and glycerol (0.5%–1.5% w/w of pectin), as plasticizer, at different casting volumes (10–20 mL). The films were used to preserve fresh strawberries	<ul style="list-style-type: none"> - At the end of the 21 days storage, strawberries protected with the films presented lower weight loss (39.1%) in comparison to unprotected fruits (43.8%); - Fruits packaged with the active films presented reduction of one Log cycle in the aerobic plate counts at 21 days of storage. 	[102]
Coating	Combination of pectin with anti-browning agents: ascorbic acid 1% (w/v), citric acid 1% (w/v) and sodium chlorite 0.05% (w/v); for apple coating	<ul style="list-style-type: none"> - Coatings were considered to be a safe and effective treatment, improving the fruit's shelf-life; - There was a reduction in microbial deterioration without significantly affecting the nutritional value of the apple. 	[103]

HM = high degree of esterification; LM = low degree of esterification.

According to the information presented in Table 3, it can be seen that pectin can act as a carrier for functional compounds in the preservation of fruits, making it possible to stop microbial growth, guaranteeing the quality of the product. However, there is still a limitation in studies on the application of edible coatings in meat products [5], as most of the research focuses on fruits, and this application should also be addressed soon.

The food industry faces many challenges to maintain the properties of processed foods. The application of pectin-based films [104], which are defined as “green” packaging due to their renewability and sustainability [96], can be highlighted as an alternative method to preserve such properties. Pectin-based films present some positive features, such as: their biodegradability, low-cost production, excellent mechanical properties, possibility to extend the shelf-life of the food packaged, and their feasibility to produce stand-alone films or incorporated with active compounds, or even combined with other polymers in blends or bilayers [104]. For example, Eça et al. evaluated the incorporation of natural extracts and vitamins in the pectin-based films could supply them with antimicrobial, nutritive and antioxidants properties. The authors concluded that the incorporation of fruits extracts in the films preserved the quality and safety of the foods packaged during their storage, while increased the antioxidant capacity [96].

Another approach that has been carried out for this same purpose is the use of bilayering technologies, based on the development of multilayer systems, which have been reported to produce films with better physical, transportation and mechanical properties as compared to those made up from a single component [88]. Gaona-Sánchez et al. produced a bilayer film by electrospraying formed by a pectin layer and a zein layer. According to the results of the authors, it is possible to produce a bilayer film, with a continuous surface structure and a well-defined interface [88].

5.2. Pectin as a Biomedical Product

As an innovative domain of biomaterials technology, studies cite pectin as a polysaccharide with promising health effects, being explored for drug delivery, gene delivery, wound healing, cholesterol reduction, tissue engineering, fabrication of membranes used in the development of contact lenses, artificial corneas, catheters, anticancer activities [5,17,18,81,105], and mucosal and gastrointestinal vehicle for drug administration and bone tissue cell vehicle [18].

The health benefits of this polysaccharide come from its composition and the presence of specific structural domains, having bioactive properties [81]. Regarding antitumor mechanisms, they are associated with their probiotic activity, immune enhancement, inhibition of tumor growth, and antimutagenic potential [13].

Due to the ability of pectin to form gels in acidic media, there is an improvement in the contact time of medications for obesity and eye treatments [106]. The ability of gels to swell under acidic conditions can benefit treatments for weight reduction and obesity. This is because when the gels reach the aqueous environment of gastric fluids, they swell and stick to the walls of the stomach before digestion, providing a feeling of satiety and lack of appetite [5]. In addition, diets rich in soluble fiber, including pectin, increase the excretion of bile acids and, consequently, result in the reduction of cholesterol, having a favorable impact in reducing the risk of cardiovascular disease [12,81].

The cholesterol-lowering properties of pectin are related to physicochemical properties, including viscosity, molecular weight, DE, and the presence of acetylation or amidation. Studies indicate that high molecular weight HM pectin lowers cholesterol levels more effectively than LM pectin [12]. The inhibition performed by pectin results from competitive inhibition with the substrate (oil/fat), entering the scene with the formation of pectin–lipase complexes. As pectin is a weak acid, it resists dissociation in the gastric environment and binds covalently to the active sites of pancreatic lipase [81].

Natural polymers are used as biocompatible and harmless carriers of drugs encapsulated in micro- or nanocapsules. Encapsulation should avoid drug degradation and promote controlled release [5]. Polysaccharides are widely used in drug delivery systems due to their ability to undergo a wide range of chemical and enzymatic reactions, forming new molecules [107]. In this sense, pectin stands out for having relatively simple gelling mechanisms, mucous adhesion, ease dissolution in basic media, ability to form gels in acidic media [5], non-toxicity, and the possibility to easily modify its functional groups (i.e., $-\text{COOH}$, $-\text{OH}$), which allows a wide application [13].

In some applications of pectin as an encapsulating agent in drug administration, HM pectins are used because they have higher molecular weight and less solubility in water. However, when encapsulating drugs with HM pectin, early release and erosion of the coating can occur. In this sense, LM pectin has been more frequently used [12]. In order to avoid early release, increase gel resistance, reduce water solubility, reduce erosion capacity and generate new materials with specific properties necessary for drug delivery, recent studies have cited the combination of pectin with other natural polymers [12,107], for example, chitosan [108], or bioactive compounds, such as curcumin [109] and cysteine [110]. Commonly, conjugates are obtained by polymerization, coupling, ligation, and synthesis in solid phase or copolymerization reactions. In addition to standard reactions, bioconjugates are also synthesized using the peptide reaction. With this, it becomes possible to obtain greater biodegradability, biocompatibility, solubility, stability, mechanical resistance, and stimulated release. Bioconjugates can also be applied in other distinct areas, such as biosensors, nanoelectronics, conductive and photonic polymers [107]. Table 4 shows some recent studies using pectin as a biomedical product.

According to the information presented in Table 4, it can be seen that pectin is capable of application as a biomedical product since it presented satisfactory results in research.

Table 4. Studies using pectin as a biomedical product.

Use of Pectin	Goal	Results	Ref
Hydrogel manufacturing	Preparation of a substance using zeolite imidazolate framework-8 (ZIF-8) nanoparticles, coated with polyethylene glycol-thioketal (PEG-TK) to manufacture SP@ZIF-8-PEG-TK nanoparticles, encapsulated with injectable hydrogel composed of sodium alginate and pectin	<ul style="list-style-type: none"> - The SP@ZIF-8-PEG-TK nanoparticles promoted the proliferation of human dermal fibroblasts, increased the expression levels of inflammation-related genes in macrophages, and exhibited favorable compatibility in vitro; - Models of full-thickness excision wounds in vivo confirmed that the dressings had excellent efficacy in wound healing. 	[111]
Hydrogel manufacturing	Preparation of pectin hydrogels loaded with theophylline for application of wound dressings and their performance of controlled drug release	<ul style="list-style-type: none"> - The concentration of the initial pectin solution is a critical parameter to obtain an effective drug release; - Dressings can be synthesized as a controlled drug delivery system. 	[112]
Development of nano-liposomal systems	Development of nano-liposomal pectin and chitosan systems for controlled delivery of neohesperidin to the gastrointestinal tract	<ul style="list-style-type: none"> - The in vitro study revealed that the systems significantly controlled the delivery of neohesperidin; - The system is considered efficient for the controlled release profile. 	[113]
Hydrogel manufacturing	Preparation of hydrogels based on pectin, lactic acid (LA), and methacrylic acid (MAA) as a potential biomaterial for colonic delivery of oxaliplatin	<ul style="list-style-type: none"> - The drug release increased with the increase in the concentration of pectin and LA, while the MAA showed the opposite behavior; - The developed hydrogels can be explored in-vivo for the colonic distribution of anticancer and other drugs. 	[105]
Coating	Production of titanium alloy discs (Ti6Al4V) coated with citrus (C) and apple (A) pectins, containing alkaline phosphatase (ALP)	<ul style="list-style-type: none"> - Pectin coatings containing ALP promoted the adhesion and proliferation of bone marrow stromal cells; - A-ALP coatings were more hydrophilic than C-ALP. 	[83]
Membrane production	Production of membrane from pectin and Aloe gel for use as a biomaterial	<ul style="list-style-type: none"> - All membranes showed high solubility (100%) and low permeability to water vapor; - The membranes produced have high potential as a biomaterial that can be used for practical applications in human health. 	[18]
Biocomposite dressings	Development of wounding dressings composed of pectin and gelatin loaded with Aloe vera and curcumin to treat wounds	<ul style="list-style-type: none"> - Biocomposite dressings are considered viable materials with strong potential for the effective treatment of wounds; - Wounds treated with pectin and gelatin matrices loaded with Aloe vera showed very fast healing, with 80% of the healing in just 8 days. 	[114]

5.3. Pectin in the Cancer Treatment

The worldwide cases of tumors registered in 2020 were 19.3 million, which resulted in 10 million deaths. It is estimated to increase 47% in these notifications by 2040 [115]. Despite continuous improvements in chemotherapy, radiotherapy, immunotherapy, and gene therapy, deaths occur mainly due to metastases. Furthermore, drug resistance exhibited by tumor cells makes therapy difficult [81].

Research with pectin and particularly with pectin decomposed into smaller fragments (MP), with lower molecular weight that the body can absorb, have demonstrated a role in the inhibition of metastasis [25,81]. Structural changes confer physical and chemical

changes in the macromolecule, which correlate with their greater bioavailability and bioactivity. MP modified with chemicals, heating, radiation, and enzymes have a deeper antitumor activity than unmodified pectin [81].

Research shows that MP comprises neutral sugar sequences with a low degree of branching and is rich in galactose. This constituent is reported to inhibit colon cancer cell growth and migration [116], due to its remarkable ability to bind to the carbohydrate recognition domain in galectin-3 (Gal3). This multifaceted and pro-metastatic protein is involved in various stages of cancer pathologies, being attractive to lead tumor cells to chemotherapy treatments [5,25,117]. The main role of Gal3 inside the cell is the regulation of apoptosis. This linkage can result in the blocking of Gal3 interactions with other proteins and peptides, resulting in the inhibition of promoting cell adhesion and migration and preventing apoptosis [25]. Therefore, unmodified pectin is considered to be too large to be absorbed and to have an effect [118].

MP, possibly loaded with cytotoxic drugs to induce apoptosis of neoplastic cells, can increase the efficiency of conventional chemotherapy [5,17]. MP is a safe and non-toxic approach to prevent or reduce carcinogenesis [25]. Studies suggest that the antitumor mechanisms of MP are correlated with its apoptosis inhibitory activity and that MP acts by sensitizing tumor cells to chemotherapeutic drugs. However, it is necessary to clarify this relationship and to characterize the structures that induce apoptosis. The establishment of a screening protocol to investigate the structure–activity relationship and the pharmacokinetics of modified pectins is necessary to optimize the Gal3 inhibitor [13].

Note that due to the ease of dissolution in basic media, resistance to proteases and amylases, and the ability to be degraded by intestinal microflora, pectin becomes appropriate for the administration of medications in the colon [5,13,119]. Soluble dietary fiber cannot be digested in the gastrointestinal tract. However, it can be degraded and fermented by the colon microbiota, reducing the risk of colon cancer [12]. Dietary pectin is fermented in the colon in short-chain fatty acids, which can normalize the intestinal microbiota, affect the galectin network, regulate apoptotic proteins in the colon's crypts, and improve the growth of the crypt colonocyte. In addition to the above, some evidence suggests that pectin can improve the immune system [13].

An annual increase in deaths from colon cancer has been reported in the literature [116]. In men, it is the third most common type of cancer, and in women, the second most common type [120,121]. Conventional treatments, such as chemotherapy and radiotherapy, have considerable disadvantages, as they do not specifically target cancer cells and can cause damage to healthy cells [122]. Currently, anticancer agents of plant origin, such as curcumin, are competitors as chemotherapy alternatives. These agents are derived from natural sources, are non-toxic even in high concentrations, and are perceived as having relatively fewer side effects [116,120,123]. However, preclinical and clinical data from oral administration of curcumin revealed its low systemic bioavailability and high susceptibility to metabolic activity, which indicates that curcumin undergoes extensive metabolic changes in the intestine and liver, which hinder the systemic utility in the treatment of cancer [116]. To overcome this restriction, several delivery vehicles have been tried to improve the bioavailability of curcumin, such as polymeric micelles, nanocomplexes, nanoemulsions, liposomes, conjugates, and lipid nanoparticles [123]. Promising drug delivery systems include drug entrapment in polymeric drug carriers, such as hydrogels and nanoparticles [121]. Among the promising curcumin nanocarriers, pectin stands out for crossing the gastrointestinal epithelium effectively and, therefore, bypassing the metabolic restrictions within the gastrointestinal tract [116].

In addition, it is worth mentioning that doxorubicin (DOX) is an effective chemotherapeutic agent widely used in the treatment of oncology. However, its effectiveness is challenged by low water solubility, rapid blood clearance, low tumor selectivity, cardiotoxicity, and cytotoxicity during chemotherapy. This is why researchers have investigated macromolecular drug delivery systems. Pectin, in this sense, has many advantages, includ-

ing good biocompatibility, biodegradable hydrophilicity properties, and adjustable release properties [124,125].

Some studies carried out in recent years using pectin in cancer treatment were compiled in Table 5.

Table 5. Studies using pectin to treat cancer.

Use of Pectin	Goal	Results	Ref
Nanocell manufacturing	Development of a pectin nanocell containing doxorubicin (DOX) for the administration of anticancer agent with reversal of resistance to multiple drugs	<ul style="list-style-type: none"> - The developed nanocell showed the expected potency against tumor growth in vitro and in vivo, significantly increasing the intracellular accumulation of doxorubicin and the prolonged release of the drug; - The nanocell reversed the drug resistance of tumor cells to some degree. 	[19]
Conjugates manufacturing	Pectin and dopamine conjugates to coordinate the ruthenium complex, as a metal model based on anticancer drugs	<ul style="list-style-type: none"> - The modification of pectin by dopamine and ruthenium complex changed the amorphous network, viscosity, and viscoelastic behavior of pectin; - Conjugates increase the prospects for the development and medical applications of new metal-based anticancer drugs. 	[126]
Coating	Development of solid double layered lipid nanoparticles coated with pectin loaded with soluble curcumin (CMN) to increase the cytotoxicity of the drug used in the treatment of colon cancer	<ul style="list-style-type: none"> - The efficiency of the nanoparticles indicated their potential application for the treatment of cancer with an increase in the bioavailability of soluble curcumin orally; - The nanoparticles showed a significantly high drug load, better stability, and a slower release profile. 	[120]
Nanoparticle manufacturing	Evaluation of the specificity and efficiency of cetuximab (Cet) conjugated to the modified citrus pectin nanoparticle and chitosan containing curcumin (MCPCNPs)	<ul style="list-style-type: none"> - The in vitro release of curcumin in a simulator medium supports the adequacy of this formulation for delivery to the colon; - The propensity to mucoadhesion of MCPCNPs was not altered after Cet conjugation; - There was superior uptake of curcumin when encapsulated in Cet-MCPCNPs. 	[127]
Nanoparticle manufacturing	Development of pectin and doxorubicin nanoparticles for the treatment of hepatocellular carcinoma	<ul style="list-style-type: none"> - The nanoparticles have achieved sustained and prolonged release capacity; - In vivo studies have shown that nanoparticles have significantly reduced the side effect of doxorubicin. 	[124]
Nanoparticle manufacturing	Development of a delivery system for modified citrus pectin and chitosan nanoparticles in the safe delivery of curcumin (MCPCNPs) for the treatment of colon cancer	<ul style="list-style-type: none"> - MCPCNPs were highly prone to mucoadhesion in the region/medium of the colon and minimal at pH 1.2 (stomach); - The data obtained suggest that MCPCNPs can be applied as a colon cancer formulation for alternative oral administration. 	[116]
Conjugates manufacturing	Preparation of a drug delivery system composed of chitosan, pectin, and doxorubicin for the treatment of liver cancer	<ul style="list-style-type: none"> - The antitumor efficiency was significantly high, demonstrated by the in vitro test; - The system effectively supplied tumor growth, according to the in vivo test; - The system is non-toxic, highly biocompatible, and safe. 	[125]

Table 5. Cont.

Use of Pectin	Goal	Results	Ref
Therapeutical compounds	Evaluation of the effectiveness of combining ionizing radiation with modified citrus pectin in prostate cancer cells	- This combination increased radiosensitivity associated with a decrease in Gal3; - Pectin significantly decreased the invasive and migratory potential of cancer cells.	[128]
Coating	Development of graphene-chitosan oxide nanocomposite coated with pectin for delivery of drugs directed to the colon	- Nanocomposites have selectively eliminated cancer cells, which indicates that it is a promising therapeutic agent for cancer treatment.	[122]
Conjugates manufacturing	Development of oral microspheres containing conjugates of pectin and doxorubicin for the treatment of colon cancer	- The conjugate of pectin and doxorubicin can be decoupled in reducing environments, resulting in cleavage of the disulfide ligands and releasing DOX; - Microspheres proved to be a promising platform for the distribution of cancer-directed doxorubicin.	[121]
Nasal spray manufacturing	Evaluation of analgesic efficacy, safety, and tolerability of fentanyl pectin nasal spray for the treatment of disruptive cancer pain	- The spray provided quick and effective pain relief, with substantial improvements in the patient life quality.	[129]
Nanoparticle manufacturing	Development of β -lactoglobulin and pectin nanoparticles for the treatment of colon cancer	- The developed nanoparticles were able to provide anticancer drugs and increase antitumor efficacy with low systemic toxicity.	[130]
Therapeutical compounds	Evaluation of the anticancer properties of pectin in vitro in breast cancer cells and in vivo using an animal model	- In vitro studies have shown that pectin can induce apoptosis, inhibit cell growth and reduce cell fixation; - In vivo studies have shown that pectin can inhibit tumor progression and increase apoptotic cells.	[131]

Table 5 depicts pectin capacity to act in cancer treatment, both in the coating of drugs and for its anticancer properties. It is observed prominence in research involving nanotherapy due to overcoming limitations associated with conventional therapeutic approaches, such as non-specificity in biodistribution, low aqueous solubility, and limited bioavailability of the asset. Lately, nanoparticles have been designed to overcome the restrictions imposed by biological barriers and offer clinical advantages over the administration of free medication in terms of flexibility in administration, toxicity, and controlled drug release capacity [122,127].

5.4. Applications in Other Segments

Given the above, it is noted that pectin has extensive applications. In addition to the information mentioned so far, note that the applications are not limited to the food, pharmaceutical, and biomedical products industries. Currently, pectins extracted from different biomass sources have been investigated as adsorbents due to their biodegradability, biocompatibility, non-toxicity, and cost-benefit ratio. Nsom et al. have developed hybrid pectin and starch nanoparticles for use as absorbents for methylene blue dye based on water recycling in the textile industry. According to the results, the nanoparticles have demonstrated efficiency and benefits such as ease of synthesis and recovery, absence of secondary pollutants, cost-benefit, and environmental compatibility [132]. Raghav et al. investigated the application of biomaterial scaffolds based on pectin and alginate inside trimetallic oxide to absorb water fluoride. According to the authors, this adsorbent is economically viable and opens a new class of adsorbents in fluoride removal studies [133].

Some studies report the use of residues, produced in large quantities every year, to extract pectin aiming at its application as a corrosion inhibitor. In this sense, there are possibilities for a positive contribution to implementing a circular economy instead of using common and toxic chemical inhibitors. Fiori-Bimbi et al. used pectin extracted from citrus peel as a corrosion inhibitor for mild steel in HCl solutions. According to the authors, pectin can be classified as a good corrosion inhibitor [134]. Grassino et al. used pectin extracted from tomato peel as a tin corrosion inhibitor. The results showed that pectin is an efficient inhibitor even at low concentrations, ranging from 53% (0.2 g·L⁻¹ concentration) to 73% (4.0 g·L⁻¹ concentration) [21].

6. Conjugates of Pectin

The union of pectin with other products is currently being investigated to improve its functional properties, including solubility, stability [135], and better antioxidant activity [109].

The protein's sensitivity to changes in pH and temperatures is a limitation for its industrial usage; thus, many studies have been done to join proteins and pectin to enhance industrial protein applications. These covalently linked molecules are known as conjugates. In this sense, the emulsifying activity of proteins was improved, using polysaccharides of high molecular weight, such as pectin, conjugated with proteins, such as lysozyme and whey protein [136].

Conjugation is one of the first stages of the Maillard reaction, in which a free amino group of the protein reacts with the carbonyl group of the reducing end of a carbohydrate [136,137]. The reaction is influenced by temperature, pH value, humidity, time, the mass ratio of the amine group and the carbonyl group, and intrinsic properties of the reactants, such as molecular weight and composition [136]. Conventional methods used for conjugation are incubating lyophilized protein-carbohydrate powders (referred to as dry heating) and aqueous protein-carbohydrate solutions (referred to as wet heating) under controlled conditions. There are also extruders, which are continuous reactors operating at flow rates of up to several hundred tons per hour and short processing times [136].

Koch et al. investigated the influence of processing conditions on whey protein conjugates and pectin production during extrusion. The authors' results suggested that processing conditions play a decisive role in the formation and degradation of the conjugate, with greater formation observed in samples treated with reverse elements and barrel temperature of 140 °C [136]. Wefers et al. also produced whey protein and pectin conjugates and concluded that the conjugates result in improved techno-functional and emulsifying properties compared with pure whey protein [137]. Qi et al. prepared conjugates between whey protein and beetroot pectin and reported that protein solubility significantly increased for the conjugates (on average 20% more than pure whey protein). Moreover, changes in the chemical composition of the protein, including the free sulfhydryl content and the level of available primary and secondary amine, were observed after the conjugation with the beetroot pectin [135].

Numerous studies on pectin complexation with other biopolymers, such as the conjugation of pectin and chitosan, are reported in the literature [107,125,138,139]. Chitosan is a cationic, biocompatible, biodegradable, and linear polysaccharide obtained from the deacetylation of chitin extracted from crustaceans [91,138]. The solubility of chitosan depends on the pH of the solvent. At low pH it can easily be dissolved, in the other hand, at higher pH, such as intestinal pH, its solubility decreases, enabling this biopolymer to be used as wall material in the encapsulation of compounds to be delivered in the intestine [108,113]. As chitosan and pectin have opposite charges. They interact through intermolecular electrostatic attractions to form a complex structure of polyelectrolytes [108]. The conjugation of these biopolymers through a chemical reaction, can improve the distribution of drugs and the controlled release profile in the upper gastrointestinal tract than using a single biopolymer [113].

Tian et al. studied the suitability of the pectin and chitosan conjugate in drug delivery systems. According to their results, the conjugate has greater thermal stability compared to native precursors. While pectin has a crystalline structure, the conjugate is more amorphous and has a semicrystalline structure [107]. Li et al. developed a macromolecule conjugated with pectin and doxorubicin and evaluated incorporating chitosan to this macromolecule. The results showed that the presence of pectin and chitosan reduced the toxicity of doxorubicin and that the conjugate containing chitosan exhibited better *in vitro* inhibition of cell growth, probably because of the incorporation of chitosan further improved cell adhesion. *In vitro* cell experiments and *in vivo* studies with animals showed that the conjugate with the addition of chitosan exhibited greater antitumor efficiency [125].

Hwang and Shin [108] produced microparticles of curcumin, chitosan, and pectin to release curcumin in the digestive system. According to the results presented, the pectin layer and the pectin crosslinking agent play a vital role in prolonging the release of curcumin, and it is found that microparticles are promising drug carriers. Bai et al. produced conjugates of pectin and curcumin with greater stability, better antioxidant activity and less cytotoxicity than free curcumin. These characteristics were attributed to the good biocompatibility of pectin [109].

Thus, it is possible to be aware that there is a wide variety of compounds that can be used in conjunction with pectin, making it possible to obtain novel properties, which can be improved and directed to specific functionalities [5].

7. Prospects, Future Trends and Challenges

Since the discovery of pectin in 1825, numerous advances have been made regarding the source of raw materials used for extraction, the extraction techniques, structural modifications, and applications of this polysaccharide [26]. Researchers interested in this area have been using the extraction optimization process to facilitate subsequent industrial applications [8,52,55,140–142].

There is a growing increase in research on pectins, which are becoming increasingly significant and widespread for different applications in the food and pharmaceutical industries and biomedical applications [26]. However, some information on stability, ideal molecular weight, and interactions with other compounds still need to be investigated. Despite the numerous researches addressing the use of pectin films in foods, only few works investigate their application for meat products [5], which may be related to the fact that pectin film can easily dissolve on this type of food due to their hydrophilic character. Thus, this can also be considered a challenge to be overcome in order to enhance the application of this films in a wider variety of foodstuffs.

Due to the ability to load and control the release of various drugs and physiological compatibility, it is perceived that pectins have an increasing demand for a renewable approach. In the future, overall development in industries is expected, as future research directions will also be based on biopolymers, biotechnologies, and renewable sources [5].

In summary, pectin can be tailor-made to generate new applications, as structural changes result in different functions and greater bioactivities. Still, it stands out that pectin can be extracted from the most varied sources, being the by-products of the food industry a green solution (due to the valorization of agro-industrial residues), which is associated with more environmentally friendly methods, allow a sustainable extraction and an environmentally friendlier product. Among the technologies described in this review, we can highlight the potential of power ultrasound technology in the degradation and oriented modification of pectin to obtain this polysaccharide with new bioactive structures and functions to be applied in the most varied areas.

Among the future challenges, the extraction of pectin without solvent or with neoteric can be highlighted to meet the fifth principle of green chemistry: Safer solvents and auxiliaries [90]. This principle must also be adopted for structural modifications of the pectin. Yet, the application of such extraction methods using green solvents are scarce in literature. Thus, there is still this gap in the knowledge to be filled, and new researches

should address the use of solvents such as deep eutectic solvent (DES), natural deep eutectic solvent (NADES) and ionic liquids (ILs).

Author Contributions: Conceptualization, C.M.P.F. and R.C.S.S.; methodology, C.M.P.F. and R.C.S.S.; resources, R.C.S.S. and J.S.R.C.; writing—original draft preparation, C.M.P.F.; writing—review and editing, J.S.R.C., V.G.L.S. and R.C.S.S.; visualization, J.S.R.C., V.G.L.S. and R.C.S.S.; supervision, J.S.R.C. and R.C.S.S.; funding acquisition, J.S.R.C. and R.C.S.S. All authors have read and agreed to the published version of the manuscript.

Funding: The authors received financial support from the National Council for Scientific and Technological Development (CNPq) and the Coordination for the Improvement of Higher Education Personnel (CAPES).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

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